

AMENDMENTS TO THE SPECIFICATION:

- **On page 32, please replace the paragraph spanning lines 19-22 with the following paragraph:**

Figures 2A-2B show the (A) light chain variable region (SEQ ID NO:205) and (B) heavy light chain variable region for an antibody sequence (SEQ ID NO:206). CDR regions are underlined. This sequence differs from the sequence disclosed in Figures 1A-1B in the first 4 residues of VH CDR1 of the light chain, residue 103 of the light chain and residue 112 of the heavy chain.

- **On page 51, please replace Table 3 with the following Table 3:**

Table 3. CDR Sequences

VH CDR1	VH CDR2	VH CDR3	VL CDR1	VL CDR2	VL CDR3
TSGMSVG (SEQ ID NO:1)	DIWWD D KK D YNPSLK S (SEQ ID NO:2)	S MI T NWYFDV (SEQ ID NO:3)	KCOLSVGYMH (SEQ ID NO:4)	DTSKL A S (SEQ ID NO:5)	FQSGGYPFT (SEQ ID NO:6)
TPGMSVG (SEQ ID NO:17)	DIWWD D KK H YNPSLK D (SEQ ID NO:18)	D MI T NFYFDV (SEQ ID NO:76)	KCOSSVGYMH (SEQ ID NO:77)	DTSYL A S (SEQ ID NO:78)	
TAGMSVG (SEQ ID NO:10)	DIWWD D KK H YNPSLK S (SEQ ID NO:79)	D MI T NWYFDV (SEQ ID NO:80)	KCOSRVGYMH (SEQ ID NO:81)	DTSYL S S (SEQ ID NO:82)	
	DIWWD D KK D YNPSLK D (SEQ ID NO:83)	D MI F NWYFDV (SEQ ID NO:29)	KCOLRVGYMH (SEQ ID NO:84)	DTKKL S S (SEQ ID NO:85)	
	DIWWD D KK H YNPSLK D (SEQ ID NO:18)	D MI F NFYFDV (SEQ ID NO:19)	KLQLSVGYMH (SEQ ID NO:86)	DTFYL S S (SEQ ID NO:49)	
	DIWWD D KK H YNPSLK S (SEQ ID NO:87)	S MI T NFYFDV (SEQ ID NO:11)	KLOSSVGYMH (SEQ ID NO:88)	DTFKL A S (SEQ ID NO:14)	
	DIWWD D KK D YNPSLK D (SEQ ID NO:89)	S MI F NWYFDV (SEQ ID NO:90)	KLOS R VGYMH (SEQ ID NO:91)	DTFKL S S (SEQ ID NO:35)	
	DIWWDG G KK H YNPSLK D (SEQ ID NO:24)	S MI F NFYFDV (SEQ ID NO:92)	KLOL R VGYMH (SEQ ID NO:93)	DTFYL A S (SEQ ID NO:94)	

	DIWWDGKKDYNPSLK S (SEQ ID NO:95) (SEQ ID NO:96)		<u>KLSLS</u> VG Y M H (SEQ ID NO:96) (SEQ ID NO:97)	DTSKLP S (SEQ ID NO:97) (SEQ ID NO:98)	
	DIWWDGKKDYNPSLK D (SEQ ID NO:37)		<u>KLSSS</u> VG Y M H (SEQ ID NO:98) (SEQ ID NO:99)	DTSGLA S (SEQ ID NO:99) (SEQ ID NO:100)	
	DIWWDGKKHYNPSLK S (SEQ ID NO:95)		<u>KLSSR</u> VG Y M H (SEQ ID NO:101)	DTSGLP S (SEQ ID NO:102)	
	DIWWD D KK S YNPSLK S (SEQ ID NO:103)		<u>KLSLR</u> VG Y M H (SEQ ID NO:104)	DTRGLP S (SEQ ID NO:27)	
	DIWWD D KK S YNPSLK D (SEQ ID NO:105)		<u>KCSLS</u> VG Y M H (SEQ ID NO:106)	DTRKLA S (SEQ ID NO:107)	
	DIWWDGKK S YNPSLK S (SEQ ID NO:108)		<u>KCSSS</u> VG Y M H (SEQ ID NO:109)	DTRGLA S (SEQ ID NO:110)	
	DIWWDGKK S YNPSLK D (SEQ ID NO:41)		<u>KCSSR</u> VG Y M H (SEQ ID NO:111)	DTRKLP S (SEQ ID NO:112)	
			<u>KCSLR</u> VG Y M H	DTMR LA S	

				(SEQ ID NO:113)	(SEQ ID NO:32)	
				<u>SLSLSVGYMH</u> (SEQ ID NO:114)	DT <u>M</u> KL <u>A</u> S (SEQ ID NO:115)	
				<u>SLSSSVGYMH</u> (SEQ ID NO:116)	DT <u>S</u> RL <u>A</u> S (SEQ ID NO:117)	
				<u>SLSSRVGYMH</u> (SEQ ID NO:21)	DT <u>S</u> LL <u>A</u> S (SEQ ID NO:118)	
				<u>SLSLRVGYMH</u> (SEQ ID NO:119)	DT <u>S</u> LL <u>D</u> S (SEQ ID NO:120)	
				<u>SCOLSVGYMH</u> (SEQ ID NO:121)	DT <u>S</u> KL <u>D</u> S (SEQ ID NO:122)	
				<u>SCOSSVGYMH</u> (SEQ ID NO:123)	DTLL <u>L</u> D <u>S</u> (SEQ ID NO:124)	
				<u>SCOSRVGYMH</u> (SEQ ID NO:125)	DTLK <u>L</u> D <u>S</u> (SEQ ID NO:126)	
				<u>SCOLRVGYMH</u> (SEQ ID NO:127)	DTLL <u>L</u> <u>A</u> S (SEQ ID NO:128)	

			<u>SLQLSVGYMH</u> (SEQ ID NO:129)	<u>DTLKLAS</u> (SEQ ID NO:130)	
			<u>SLOSSVGYMH</u> (SEQ ID NO:131)	<u>DTSKLSS</u> (SEQ ID NO:132)	
			<u>SLOSrvGYMH</u> (SEQ ID NO:133)	<u>DTSKOAS</u> (SEQ ID NO:134)	
			<u>SLQLRVGYMH</u> (SEQ ID NO:135)	<u>DTSKOSS</u> (SEQ ID NO:136)	
			<u>SCSLSVGYMH</u> (SEQ ID NO:137)	<u>DTSYLAS</u> (SEQ ID NO:138)	
			<u>SCSSSVGYMH</u> (SEQ ID NO:139)	<u>DTSYLSS</u> (SEQ ID NO:140)	
			<u>SCSSRVGYMH</u> (SEQ ID NO:141)	<u>DTSYQAS</u> (SEQ ID NO:142) (SEQ ID NO:143)	
			<u>SCSLRVGYMH</u> (SEQ ID NO:143)	<u>DTSYQSS</u> (SEQ ID NO:144)	

			(SEQ ID NO:142)	
			<u>DTMYQAS</u> (SEQ ID NO:146)	
			<u>DTMYQSS</u> (SEQ ID NO:43)	
			<u>DTMKOAS</u> (SEQ ID NO:149)	
			<u>DTMKQSS</u> (SEQ ID NO:151)	
			<u>DTMYLAS</u> (SEQ ID NO:153)	
			<u>DTMYLSS</u> (SEQ ID NO:155)	
			<u>DTMKLAS</u> (SEQ ID NO:157)	
			<u>DTMKLSS</u> (SEQ ID NO:159)	
			(SEQ ID NO:144)	
			<u>KPSSRVGYMH</u> (SEQ ID NO:145)	
			<u>KPSLRVGYMH</u> (SEQ ID NO:147)	
			<u>KPSSSVGYMH</u> (SEQ ID NO:148)	
			<u>KPSLSVGYMH</u> (SEQ ID NO:150)	
			<u>KPOSRVGYMH</u> (SEQ ID NO:152)	
			<u>KPOLRVGYMH</u> (SEQ ID NO:154)	
			<u>KPOSSVGYMH</u> (SEQ ID NO:156)	
			<u>KPOLSVGYMH</u> (SEQ ID NO:158)	

			<u>SPSSRVGYMH</u> (SEQ ID NO:160)	<u>DTSKLSS</u> (SEQ ID NO:161)	
			<u>SPSLRVGYMH</u> (SEQ ID NO:162)	<u>DTRYOAS</u> (SEQ ID NO:163)	
			<u>SPSSSVGYMH</u> (SEQ ID NO:164)	<u>DTRYOSS</u> (SEQ ID NO:164)	
			<u>SPSLSVGYMH</u> (SEQ ID NO:165)	<u>DTRKOAS</u> (SEQ ID NO:166)	
			<u>SPOSRVGYMH</u> (SEQ ID NO:167)	<u>DTRKQSS</u> (SEQ ID NO:168)	
			<u>SPQLRVGYMH</u> (SEQ ID NO:169)	<u>DTRKLAS</u> (SEQ ID NO:170)	
			<u>SPOSSVGYMH</u> (SEQ ID NO:171)	<u>DTRKLSS</u> (SEQ ID NO:172)	
			<u>SPQLSVGYMH</u> (SEQ ID NO:173)	<u>DTRYLAS</u> (SEQ ID NO:174)	
			<u>KAOSRVGYMH</u> (SEQ ID NO:175)	<u>DTRYLSS</u> (SEQ ID NO:177)	

			<u>KAQLRVGYMH</u> (SEQ ID NO:176)			
			<u>KAQSSVGYMH</u> (SEQ ID NO:178)			
			<u>KAQLSVGYMH</u> (SEQ ID NO:179)			
			<u>KASSRVGYMH</u> (SEQ ID NO:180)			
			<u>KASLRVGYMH</u> (SEQ ID NO:181)			
			<u>KASSSVGYMH</u> (SEQ ID NO:182)			
			<u>KASLSVGYMH</u> (SEQ ID NO:183)			
			<u>SASSRVGYMH</u> (SEQ ID NO:39)			
			<u>SASLRVGYMH</u> (SEQ ID NO:184)			

				<u>SASSSVGYMH</u> (SEQ ID NO:13)		
				<u>SASLSVGYMH</u> (SEQ ID NO:185)		
				<u>SAOSRVGYMH</u> (SEQ ID NO:186)		
				<u>SAQLRVGYMH</u> (SEQ ID NO:187)		
				<u>SAOSSVGYMH</u> (SEQ ID NO:188)		
				<u>LPSSRVGYMH</u> (SEQ ID NO:47)		
				<u>LPSLSVGYMH</u> (SEQ ID NO:189)		
				<u>LPSSSVGYMH</u> (SEQ ID NO:190)		
				<u>LPSLRVGYMH</u> (SEQ ID NO:191)		

			<u>LCSSRVGYMH</u> (SEQ ID NO:192)			
			<u>LCSLSVGYMH</u> (SEQ ID NO:193)			
			<u>LCSSSVGYMH</u> (SEQ ID NO:194)			
			<u>LCSLRVGYMH</u> (SEQ ID NO:195)			
			<u>LPQSRVGYMH</u> (SEQ ID NO:196)			
			<u>LPOLSVGYMH</u> (SEQ ID NO:197)			
			<u>LPQSSVGYMH</u> (SEQ ID NO:198)			
			<u>LPQLRVGYMH</u> (SEQ ID NO:199)			
			<u>LCOSRVGYMH</u> (SEQ ID NO:200)			

			<u>LCQLSVGYMH</u> (SEQ ID NO:201)		
			<u>LCQSSVGYMH</u> (SEQ ID NO:202)		
			<u>LCQLRVGYMH</u> (SEQ ID NO:203)		
			<u>SAQLSVGYMH</u> (SEQ ID NO:204)		

- On page 117, please replace Table 5 with the following Table 5:

Table 5.

<u>Monoclonal Antibodies vs Bac-F (1:1)</u>				
	<i>K_{on}</i> (x E+5)	<i>K_{off}</i> (x E-5)	K_D (nM)	Chi2
P12F2	4.07	12.8	0.31 (13)	0.9
P12F4	4.95	5.55	0.11 (35)	0.6
A13c4	3.00	3.96	0.13 (30)	1.2
A12a6	4.60	1.65	0.04 (98)	1.2
A1e9	4.33	14.3	0.33 (12)	2.5
A8c7	4.17	8.75	0.21 (19)	1.8
P11d4	4.66	28.9	0.62 (6)	1.0
A17d4	4.56	4.07	0.09 (43)	0.5
A4B4(1) (Sequence not shown)	4.34	1.06	0.02 (195)	1.5
SYNAGIS®	1.32	51.5	3.90 (1)	0.6

- On page 118, please replace Table 6 with the following Table 6:

Table 6.

<u>Monoclonal Antibodies vs NUF4 (1:1)</u>				
	<i>K_{on}</i> (x E+5)	<i>K_{off}</i> (x E-5)	K_D (nM)	Chi2
P12F2	5.41	17.8	0.33 (26)	1.2
P12F4	9.43	22.9	0.24 (36)	0.9
A13c4	3.65	27.2	0.75 (12)	1.8
A12a6	4.00	29.1	0.73 (12)	1.9
A1e9	8.43	58.4	0.69 (13)	0.9

A8c7	8.25	53.5	0.65 (13)	0.7
P11d4	9.04	76.6	0.85 (10)	2.5
A17d4	4.99	36.2	0.73 (12)	2.0
A4B4(1) (Sequence not shown)	4.96	28.2	0.57 (15)	1.9
SYNAGIS®	3.04	265	8.70 (1)	0.4

- On page 118, please replace Table 7 with the following Table 7:

Table 7.

	<u>Monoclonal Antibodies vs NUF4 (2:1)</u>			
	K_{on} (x E+5)	K_{off} (x E-5)	K_D (nM)	Chi2
P12F2	2.82	23.6	0.84 (371)	1.5
P12F4	2.73	63.6	2.33 (134)	4.9
A13c4	3.20	22.5	0.70 (446)	1.7
A12a6	2.18	40.8	1.87 (167)	1.9
A1e9	3.29	139	4.22 (74)	2.8
A8c7	4.30	114	2.65 (118)	2.0
P11d4	3.66	313	8.55 (36)	3.6
A17d4	2.64	29.2	1.11 (281)	1.7
A4B4(1) (Sequence not shown)	2.03	40.06	2.00 (156)	1.4
SYNAGIS®	0.78	2420	312 (1)	1.3

- On pages 118-119, please replace the paragraph spanning page 118, line 35 – page 119, line 7 with the following paragraph:

1X-493L2FR, H3-3F4, M3H9, Y10H6, DG, *AFFF, 6H8, L1-7E5, L2-15B10, *P12F2, *P12F4, *P11d4, *Ale9, *A12a6, *A13a11, and *A13c4 are Fab fragments having the framework sequences of ~~Figure 1~~ Figure 2 and the ~~indicated~~ CDR sequences indicated listed in Table 2. ~~SYNAGIS®, AFFF, P12F2, P12F4, P11d4, Ale9, A12a6, A13c4, A17d4, A4B4 and A8c7 are actual monoclonal antibodies~~ SYNAGIS® is a monoclonal antibody with the framework sequences of Figure 1 and constant regions as described in Johnson et al. (1997, Journal of Infectious Diseases 176:1215-1224) and U.S. Patent No. 5,824,307. The framework sequences of these ~~antibodies~~ this antibody may differ slightly from those of the Fab fragments.

- On pages 120-121, please replace Table 8 with the following Table 8:

Table 8. End Point RSV Microneutralization Titer Of High On Rate Mutant IgG and Fab

Molecule	Mean IC50 (Curve) µg/ml	STDEV Curve IC50	Fold Difference (Curve ICX50)	Mean IC50 (Control) µg/ml	STDEV Control IC50	Fold Difference (Control IC50)	n (assay repeat)
SYNAGIS®	0.4527	0.208	-	0.5351	0.238	-	8
**Ale9	0.0625	0.0268	7	0.0645	0.0223	8	3
**A17d4	0.0342	0.022	13	0.0354	0.0187	15	4
**P11d4	0.0217	0.0331	21	0.0289	0.0110	19	5
**P12F2	0.0231	0.0141	20	0.0223	0.0083	24	6
**A8c7	0.0337	0.0309	13	0.0383	0.0283	14	5
**A12a6	0.0357	0.0316	13	0.0354	0.0261	15	7
**P12F4	0.0242	0.0163	19	0.0235	0.0076	23	7
**A13c4	0.0376	0.0268	12	0.0375	0.0213	14	6
**A4B4(1) (Sequence not shown)	0.0171	0.0018	27	0.0154	0.00417	35	2
*Ale9	0.157	-	3	0.125	-	4	1
*A17d4	0.0179	-	25	0.0171	-	31	1

*P11d4	>1.00	-	-	>1.00	-	-	1
*P12F2	0.0407	0.0112	11	0.0326	0.00905	16	2
*A8c7	0.177	-	3	0.157	-	34	1
*A12a6	0.0287	0.00417	16	0.0310	0.00982	17	2
*P12F4	0.0464	0.00791	10	0.0351	0.0126	15	2
*A13c4	0.0264	0.00141	17	0.0258	0.00071	21	2
*A4B4(1) (Sequence not shown)	0.0414	-	11	0.0411	-	13	1
*A13a11	0.120	0.0222	4	0.1022	0.0260	5	2
*A1h5	0.194	0.462	2	0.176	0.0625	3	2

** Monoclonal Antibody

* Fab Fragment

• On page 122, please replace the paragraph spanning lines 11-18 with the following paragraph:

Antibodies having the amino acid sequence of A13c4, A17d4, A4B4 A4B4(1) (sequence not shown), and SYNAGIS® were diluted in dialysate and the concentrations were determined by UV spectroscopic absorption measurements with a Perkin-Elmer Lambda 4B Spectrophotometer using an extinction coefficient of 217,000 M⁻¹ cm⁻¹ at the peak maximum at 280 nm. The diluted NUF4 concentrations were calculated from the ratio of the mass of the original sample to that of the diluted sample since its extinction coefficient was too low to determine an accurate concentration without employing and losing a large amount of sample.

• On page 123, please replace the paragraph spanning lines 21 – 34 with the following paragraph.

The ITC results are summarized in Table 9. The higher than 2 stoichiometries in Table 9 indicate that either the concentration determination of the antibody or NUF4 was

incorrect. Since the same NUF4 sample was used as a titrant with antibodies having the amino acid sequence of A13c4 at 35°C and A17d4 at 35°C, which exhibit in at least one of the titrations the correct stoichiometry of 2, it is assumed that the titrant concentration was correct and that the large values of n result from incorrectly determined antibody concentrations. However, it can be shown that the binding constants are critically dependent on the titrant concentration and, thus, despite the 2-3 disparity in n, the binding constants are correct. Since the binding constants of antibodies having the amino acid sequence of A4B4(1) (sequence not shown) and A13c4 at 25°C were near the upper determination limit by ITC (equation 2) and with the limited amount of available NUF4, it was decided to use 35°C as the reference temperature for comprising the binding affinities. The results summarized in Table 9 show that the binding affinities to NUF4 are in the order A4B4(1) > A13c4 > A17d4 > SYNAGIS®.

- On page 123 - 124, please replace Table 9 with the following Table 9:

Table 9. Average Binding Constants and Enthalpies of NUF4 to Antibodies

Antibody	K_b	ΔH_b in kJ mol^{-1}
A4B4(1) (Sequence not shown)	$269 \pm 74 \times 10^6 \text{ M}^{-1}$ or $\sim 3.7 \text{ nM}^*$	92.8 ± 1.0
A13c4	$107 \pm 28 \times 10^6 \text{ M}^{-1}$ or 9 nM	67 ± 17
A17d4	$75 \pm 14 \times 10^6 \text{ M}^{-1}$ or 13 nM	68 ± 10
SYNAGIS®	$1.23 \pm 0.17 \times 10^6 \text{ M}^{-1}$ or 810 nM	71 ± 5

* Based only on the best titration run at 35°C.

4.0 nM is ITC lower limit of $1/K_b$ range (ITC range is limited to $[\text{antibody}]_n K_b = 500$ where n is the stoichiometry and $[\text{antibody}]$ is the concentration of the antibody in the cell).

- Between pages 127 and 128, on a separate page, please replace the Sequence Listing with the Sequence Listing submitted herewith.